proportion of positive results in the conditions indicated is in general much higher than the incidence of high total globulin values or of changes in the albumin–globulin ratio. On account of the non-specific nature of the tests they must always be interpreted with due regard to the general clinical background, a proviso which would of course apply to most laboratory investigations.

As regards the relative merits of the various tests there is room for considerable difference of opinion. However, from the physico-chemical angle it can be said that the conditions are more accurately controlled in the case of the thymol and colloidal-gold tests, in which the pH and ionic strength are kept at optimum levels by means of buffer solutions. Study of purely clinical data suggests that the gold, thymol, and cephalin–cholesterol tests all have certain advantages, but in the study of liver disease the thymol test appears at present to be slightly superior. It also has the advantage that the reagent is easier to prepare than either of the other two. Most of the other tests mentioned are probably not so reliable as " liver function tests " but have found useful applications in the study of certain infections. The position of the sharlach-red and zinc-sulphate turbidity tests needs to be elucidated by further study.

There is a certain advantage for routine purposes in using two tests of slightly different character, and my present preference is for the thymol (turbidity and flocculation) and the gold tests. The former is fairly specific for liver disease, the latter gives a greater sensitivity in conditions such as rheumatoid arthritis. However, the gold test might well be replaced by the cephalin–cholesterol test or possibly one of the other tests if difficulty is experienced in making up the gold sol. All the tests are so similar in principle that it is to be hoped that some degree of standardization will be eventually achieved ; the ideal would be a single accepted test for demonstrating gamma-globulin excess.

Summary

The chemical mechanism underlying the various flocculation tests has been considered, and the essential similarity of these tests is emphasized.

All the tests are influenced positively by serum gamma-globulin and negatively by albumin. The alpha- and beta-globulin fractions do not influence the thymol test but have a variable effect on the others.

The formol-gel and $ZnSO_4$ tests are closely correlated with total serum globulin, the others have little correlation with total globulin.

The relative value of the various tests as indicators of hepatic dysfunction and of antibody formation is discussed.

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THE CONSERVATIVE TREATMENT OF PLACENTA PRAEVIA

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In every discussion on the treatment of placenta praevia there are two fundamental questions to be answered— namely, what to do and when to do it. The former has fortunately been simplified with the increasing safety of the lower-segment caesarean operation, and the procedure of choice will usually be either rupture of membranes or abdominal delivery. However, the optimum timing of this intervention remains a matter of opinion on which authorities are at variance. It has long been taught, with considerable emphasis in many schools, that expectant treatment of a diagnosed or suspected placenta praevia can never be countenanced. This principle has been based upon the not unnatural supposition that a patient with a major degree of placenta praevia would in the absence of intervention frequently bleed to death, and that fatal haemorrhage might ensue at any time without warning. Evidence is accumulating, however, to suggest that more tragedies are produced nowadays by overtreatment than by neglect, and that in some cases delay might even benefit mother as well as foetus ; for in the borderline case rupture of forewaters can be performed with far more confidence when it has been possible to delay until the uterus is contracting and the cervix open.

An American obstetrician (Johnson, 1946), in an enthusiastic overstatement to prove his case, has promised a reward for records of any case of placenta praevia in which death from haemorrhage has followed strict non-intervention in all stages of labour. It has apparently not been claimed, but this does not necessarily prove anything, since no doctor could remain idle in expectation of seeing his patient die from haemorrhage. This helps to emphasize the fact that there are natural ways of arrest of haemorrhage from a placenta praevia. In rare instances the placenta may actually be delivered spontaneously in front of the foetus with remarkably slight blood loss (Lloyd, 1947, reported below). It cannot be denied that some cases of placenta praevia have sudden haemorrhages which may be most alarming and require urgent blood transfusion if the uterus is not emptied as a routine as soon as the condition is suspected. On the other hand, a period of delay *might* facilitate treatment and decrease the number of caesarean sections, and it assuredly *will* lower the appalling foetal loss from prematurity.

A brief review will be given of the recent pertinent literature and a series of 100 cases presented in an effort to assess the advantages and risks to mother and child that may be expected with conservative treatment.

Recent Literature

Probably the finest series of cases in which treatment was based strictly on the old principle of immediate intervention was reported from Chicago by Davis and Campbell (1946). Treatment was generally confined to caesarean section or rupture of the membranes according to the position of the placenta as felt on vaginal examination shortly after the patient had been admitted to hospital; maternal mortality was as low as 0.6% (two deaths in 325 cases), which compares extremely favourably with the figure of 5.9% compiled by Professor F. J. Browne (1946) from 3,103 cases in recent records of 11 British teaching hospitals. The caesarean section rate was 40%, and blood transfusion was given to 40% of patients (a high figure). Quoting a foetal mortality of 32%, the authors state that "the most important cause of foetal death was prematurity," and "the premature infant has been considered expendable to ensure the greatest possible safety for the mother." Although this figure for foetal loss is decidedly better than that of 54.2% in Browne's series, it is not nearly low enough; and other authorities claim that judicious conservatism will give equally good maternal results with considerably improved chances for the baby.

Expectant treatment was championed simultaneously on both sides of the Atlantic by Macafee (1945) and Johnson (1945). Both based their treatment on the contention that *in the absence of vaginal manipulation* the first haemorrhage from a placenta praevia will never be fatal, and subsequent haemorrhages will not be fatal so long as the haemoglobin level of the blood is normal at the onset of bleeding. Macafee reported a personal series of 174 cases with one death and a foetal loss of only 23.5%; yet this figure included six foetal abnormalities and nine other cases in which the low implantation of umbilical cord into placenta made foetal death almost inevitable after a severe haemorrhage: an improved figure for foetal loss of only 6% was achieved in the last 47 cases. This revolutionary conception of foetal risk was attained by extreme conservatism: the principle was laid down that no vaginal examination should be made unless and until it could be followed immediately by whatever treatment was required for delivery (e.g., caesarean section). Thus a patient would be put to bed to wait until the last few weeks of pregnancy, regardless of repeated "warning" haemorrhages so long as there was no undue anaemia; and with increasing experience there was less cause for alarm over any one apparently severe attack of bleeding. Macafee states significantly that "among these patients there has been nothing to confirm the belief that recurrent haemorrhages tend to lead up to one catastrophic haemorrhage." He permitted a period of delay in over half the cases, one patient spending 14 weeks in hospital, while another had nine attacks of bleeding; yet blood transfusion was required in only 13% of patients, and 39% (not a high figure) were delivered by caesarean section.

Johnson (1945) treated 79 cases of placenta praevia without a maternal death and with loss of 22% of babies. His relatively high (53%) caesarean section rate is an index of his reluctance to interfere vaginally in any way at all, and his dictum, "a non-traumatized placenta praevia will not cause fatal haemorrhage," sums up his general attitude.

In an attempt to check the validity of Macafee and Johnson's contentions, Yepes and Eastman (1946) summarized 304 cases that had been treated during the past half-century along conventional lines in the Johns Hopkins Hospital. The maternal mortality had been reduced during the period from 13.8% to 0.9%, but the foetal loss had improved only from 78.5% to 46.8%. They found that in no instance had an initial or subsequent haemorrhage been the cause of death except in association with extensive vaginal manipulation; and that the only patient to die undelivered (in 1920) had refused treatment, had become profoundly anaemic from four subsequent attacks of haemorrhage at home, and had finally died after vaginal manipulations.

Daichman and Pomerance (1947) reported a series of 165 cases over an eleven-year period, with one maternal death and a foetal loss of 26%. They attribute their good results to a rather liberal use of caesarean section (59%) and a gradual increase in expectant treatment. They consider that it is safe to temporize "when the infant is near viability," implying that repeated haemorrhage is less likely to occur before the last few weeks of gestation: this may not be altogether true, but it serves to underline their approval of at least a limited conservatism.

Finally, Williams (1948) reported a series of 105 cases with only one maternal death over an eleven-year period; the foetal loss was 28% and the caesarean section rate 42%. However, there were 41 cases (39%) treated expectantly, and of these the foetal mortality was only 12%. He thus endorses the great improvement in foetal chances of survival that may be expected with this treatment.

After such apparent success of varying degrees of conservative treatment it was disappointing to hear reactionary views from Scotland expressed by Sturrock, Stirling, and Tennent (1947). A series of 228 cases was quoted from Edinburgh with only two maternal deaths but a foetal loss of 39%; conservative treatment had been practised in 6%, and the authors express no enthusiasm for it on account of "the close vigilance required and the smooth and speedy application of appropriate treatment essential in the presence of the sudden further haemorrhage." The Glasgow school, quoting 505 cases, in 27% of which there had been at least 24 hours' delay before instituting active treatment, was very discouraging: the overall figures showed 18 maternal deaths, 34% foetal loss, and 55% caesarean sections, while in the delayed group there was a slightly higher foetal loss with considerably greater maternal morbidity. The significance of these results may perhaps be offset by the selection of their group for delayed treatment, so that direct comparison of results between the two groups is not applicable. Another factor that might have affected the expectant group adversely is a variation from the more usual management of this type of case: vaginal examination of the more serious cases was conducted under anaesthesia in only 1 or 2% of patients.

To conclude this summary of available evidence it may be stated that most of the obstetricians who have reported their experiences of the expectant treatment of placenta praevia appear to have been favourably impressed with the results.

Personal Experience

In the following report a small series of cases has been analysed in an attempt to ascertain how nearly the results of Macafee and Johnson can be equalled in a busy hospital in which responsibility for emergencies devolves upon all members of the honorary staff. It is obvious that the principles of conservative delay (with its worries and disadvantages) are unlikely to be accepted as quickly and comprehensively as when all experience is gained and all responsibility accepted by one man. It is therefore encouraging to record a consecutive series of 100 cases of placenta praevia (95 in 1947 and 5 in 1948) treated at

the Birmingham Maternity Hospital by six members of the staff with no maternal deaths and the loss of only 17 out of 103 babies (stillbirths and neonatal deaths in hospital). There had been no maternal death from placenta praevia in the three years prior to this series.

The principles of treatment were as follows. There was general agreement among the staff that so far as possible no infant should be delivered before about the 37th week of gestation, although, if the foetus appeared to be very well developed and there were other indications, a week or two earlier might be allowed. After the 37th week it was considered that the risks to the foetus of asphyxia following a severe haemorrhage, and the now unnecessary loss of blood to the mother, outweighed the advantages of the last few possible weeks *in utero* ; consequently a severe haemorrhage in the last three or four weeks was considered an indication to empty the uterus: before this it called for conservative treatment. However, there was considerable divergence of opinion among the staff about the wisdom of continued delay in the face of repeated haemorrhage, and inevitably there were occasions on which active intervention was deemed advisable in maternal interests when another surgeon might have advised procrastination still further.

The usual procedure in the case of haemorrhage before the 37th week was to admit the patient to hospital, examine the cervix with a speculum, give morphine as required, and wait for bleeding to stop ; the haemoglobin level was checked, the blood grouped and the rhesus test performed, and blood cross-matched for transfusion in the more serious cases. After several days without further loss primigravid patients were often sent home to bed, and most cases with only a slight loss before the 32nd week were allowed up and sent out with instructions that in the event of further haemorrhage they should go straight to bed and discourage any vaginal examination. No attempt was made at radiographic diagnosis of the placental site. No vaginal examination was to be made in hospital until the formal procedure under an anaesthetic with the theatre set for caesarean section, generally after the 36th week. The date of this examination depended on the size of the baby, the recurrence of haemorrhage, and the attitude of the surgeon to repeated blood loss ; and also on the reaction of the foetal heart to each attack of haemorrhage. As a general rule the procedure adopted was caesarean section for cases in which the placenta was palpated across the cervix or coming up to its margin (the second, third, and fourth degrees of Professor F. J. Browne), with rupture of membranes for the others. Sometimes a second-degree case in a multipara would be treated by rupture of membranes with application of Willett's forceps to the scalp, or bringing down a leg of a flexed breech if this could be done easily through a dilating cervix ; thus one would be able to exert traction on the presenting part should the bleeding be uncontrolled. Bipolar version and subsequent breech extraction was employed only twice, on patients whose babies were already dead.

The anaesthetic for the examination was generally thiopentone, and it was usually followed by gas–oxygen–ether or " trilene " for the section ; a number of severe cases in which the diagnosis appeared self-evident, however, were operated on under spinal or local analgesia without any vaginal examination in an effort to avoid further foetal distress. The lower-segment operation was generally used. Blood transfusion was given freely, being set up before the vaginal examination in all cases of dangerous haemorrhage: it was used in 21 cases, including three occasions for post-partum haemorrhage following vaginal delivery. Statistics are given in Table I.

Conservative Treatment

Macafee quotes a figure of over 50% for cases of placenta praevia in which conservative treatment was practicable. This was by no means so in the series under consideration. There were two reasons: in the first place, the majority of patients had already experienced one or more attacks of bleeding before admission, and successful (though often ill-advised and hazardous) conservative treatment had been practised by their practitioners ; consequently the majority of those admitted were already in the last month of pregnancy. Secondly, a distressingly large number of patients had already been examined

vaginally outside hospital, and this misplaced active intervention had often produced serious exacerbation of haemorrhage and sometimes foetal distress. There were in fact only 26 patients (27 babies) admitted with bleeding before the 36th week, and as one patient was already in labour and two babies were dead there were only 24 cases in which it is considered that planned conservative treatment was possible. These are summarized in Table II.

TABLE I.—*Statistical Summary*

Cases of placenta praevia	100	
Babies delivered	103	
Maternal deaths	0	
Foetal and neonatal loss	17 (16·5%)	
Types of placenta :		
1st degree	43	
2nd „	28	
3rd „	25	
4th „	4	
Primigravidae	32	
„ with 1st degree placenta praevia ..	19 (59%)	
Treatment:		
Caesarean section (including 2 following A.R.M.) ..	47	
A.R.M. alone	22	
A.R.M., Willett's forceps*	5	
A.R.M., bringing down leg*	5	
Internal version and extraction	2	
Non-intervention†	14	
Forceps delivery†	4	
Craniotomy†	1	

* Subsequent traction rarely required.
† No treatment needed for haemorrhage.

TABLE II.—*Conservative Treatment*

Conservatism possible	24	
„ not used	4 (foetal loss 3)	
„ attempted	20 („ „ 3)	
„ abandoned within 7 days	4 („ „ 0)	
„ persisted for over 7 days	16 („ „ 3)	

Maternal Prognosis

The maternal prognosis under the conservative regime has not apparently deteriorated in any way, and in very few cases was there ever cause for the slightest alarm ; this may have been partly due to a natural reluctance to continue procrastination in the face of repeated bleeding, but the morale of the resident staff, as well as the safety of the patients, was certainly maintained by a good supply of readily available blood for transfusion. On several occasions there was a sudden loss of 15–20 oz. (425–570 ml.) of blood, usually in the middle of the night, but experience soon confirmed Macafee's statement that these haemorrhages are not catastrophic. In fact it can be categorically stated that in no instance was maternal life endangered by conservative treatment: there were no deaths and no " near deaths." In the 16 cases in which conservatism was practised for a week or more, in hospital or after discharge home, the maximum period of delay was 8 weeks and the average 17 days. Of the four cases in which active treatment was adopted in less than a week two had recurrent haemorrhage, one had pre-eclamptic toxaemia, and one had spontaneous premature labour.

Foetal Prognosis

The reduction of foetal loss is the real justification of conservative treatment, and the figure of 16.5% compares favourably with F. J. Browne's collected figure of 54% and with other series where active intervention has been adopted. That the improvement chiefly affects the premature component of the foetal death rate is shown by the 24 quoted cases in which the patient was admitted before the 36th week and conservatism was possible: when it was practised the loss was 15%, and when it was neglected the loss was 75%. The whole subject of foetal death in relation to placenta praevia is so important that an analysis has been made of the cases in this series, and an effort has been made to determine how far foetal

TABLE III.—*Analysis of the 17 Foetal Deaths*

Associated with prematurity	6	
Possible mismanagement	5	
Misfortune	1	
Apparently inevitable	5	

mortality may be reduced by conservative strategy and skilled tactics and what may be the hard core of inevitable loss. Table III gives a rough classification of the 17 cases.

In any discussion on the inevitability or otherwise of foetal death it is essential that outside practitioners and hospital staff should be considered together as one therapeutic unit. In no

case should loss of a baby be classed as inevitable on the grounds that the damage was done before admission to hospital, and it is only by a consideration of the mistakes of the practitioners, as well as the possible accidents or errors committed inside hospital, that a true estimate of optimum foetal prognosis may be made.

There were six foetal deaths associated with prematurity, and four of these patients had had vaginal examinations which had precipitated further bleeding before admission ; in one case the foetus was dead on admission and in another the patient was already in labour, though it is difficult to be certain how far these facts are attributable to intervention. In the other two cases which had already been examined it was decided that conservative delay was unlikely to be successful, and both were examined under anaesthesia, followed by section for one and rupture of membranes for the other. Of the two patients who had had no intervention, one was kept in hospital for two weeks (29th to 31st) and then delivered because of repeated minor haemorrhage ; the other (at the 34th week) was delivered at once. Both had caesarean sections and both infants died as the result of prematurity. It is probable that if intervention had been longer delayed the chances of survival of these two infants would have been materially increased, with little, if any, added maternal risk.

It is unfortunately necessary to record five cases in which foetal death followed mismanagement in some stage of the patient's treatment either by the practitioner outside or by the resident staff in hospital. The first, a 3-gravida with no living children, had four " warning " haemorrhages in the last month of pregnancy before a final severe bleeding for which she was admitted in labour at term ; there was profound foetal asphyxia, and despite immediate caesarean section the child failed to survive. At operation it was found that the cord was inserted into the placenta immediately over the internal os. This case serves to emphasize that in the last weeks of pregnancy conservative treatment may not be in the interest of the foetus. The second case illustrates the same lesson. A 2-gravida was admitted following an initial severe haemorrhage at the 38th week. There was no foetal distress, and examination was delayed on account of other supposedly more urgent work, but three hours later the foetal heart rate fell to 104 and caesarean section, though urgently performed, failed to save the child ; it lived for a few hours, and necropsy showed severe asphyxial changes in the viscera. The third case (reported elsewhere, Mills, 1948) was one of vaginal delivery of a multipara despite a third-degree placenta praevia. Premature rupture of membranes without bleeding had led to the erroneous conclusion that the os must be at least partly covered by membranes, and the patient was delivered by traction on Willett's forceps, which controlled bleeding but asphyxiated the baby. Finally, there were two cases in which bad technical errors were made. A baby was lost from cerebral haemorrhage during forceps extraction at the 36th week following two weeks' successful conservative treatment of a primigravida ; and a foetus died from asphyxia in the first stage of labour owing to compression of a posterior placenta praevia by the descending head in a primigravid patient in whom placenta praevia had not been suspected. These five cases represent five unnecessary foetal deaths.

The one case of " misfortune " was an 8-lb. (3.63-kg.) baby which died from neonatal infection when a fortnight old.

There were five cases in which foetal death appears to have been unavoidable. Two of these were cases of vasa praevia, in one of which only the first of twins was lost, while in the other there was no haemorrhage until the presenting vessel was torn with the rupture of the membranes early in labour. There was one hydrops foetalis. One case appeared to be an association of placenta praevia with accidental retroplacental haemorrhage and rapid foetal asphyxia. The final case (reported elsewhere, Lloyd, 1947) was one in which the placenta became fully separated early in labour with no alarming haemorrhage and was found lying loose in the vagina at examination for an impacted shoulder presentation.

There is thus reason to believe that with good luck, more skilful management, and a more resolute adoption of conservative principles the foetal loss in the cases outlined above might have been reduced from 17 to 7 without in any way increasing the maternal dangers.

Conclusions

The number of cases of placenta praevia in which it is possible and advisable to adopt conservative measures depends upon the stage in pregnancy at which the patient is sent to hospital for advice. If this is sought after the first haemorrhage, and there has been no previous intervention, Macafee's experience shows that deferring of active treatment may be practicable in over 50% of cases ; but if, as is shown in this series, there has already been procrastination or examination before admission, then this number may be reduced to about 25%.

Conservative treatment has advantages and disadvantages for the mother ; the latter are the more obvious. She must either be confined to hospital or lead a very restricted existence at home for a number of weeks, and she may sometimes be required to suffer further haemorrhage ; on the other hand, there is little, if any, increased danger to life, and there is a slightly lower chance of the need for delivery by caesarean section. If, however, caesarean section should eventually become necessary there is a much greater probability that she will get a live baby in compensation.

The advantages to the foetus of conservative delay greatly outweigh the risks, since maturity is the prime requisite for foetal survival. However, it must not be forgotten that any serious haemorrhage may suddenly produce foetal asphyxia, and consequently delay of even a few hours is unjustifiable when the foetus has reached a satisfactory stage of development. Since conservative treatment has been adopted for placenta praevia the published reports show for the first time a foetal and neonatal loss below 30%.

Finally, it is considered that the careful adoption of conservative measures in suitable cases is practicable only in a hospital serving an area blessed with reasonably good transport facilities, a good blood-transfusion service, and an adequate standard of general nutrition among its patients ; further, it will naturally require a sufficiency of antenatal beds and an experienced resident staff. In these circumstances, given co-operation from the local practitioners, there is every opportunity for the reduction of foetal mortality in placenta praevia to a figure in the region of 10% while the maternal mortality remains at its present minimal figure.

Summary

Recent literature relative to the conservative treatment of placenta praevia is reviewed.

A series of 100 cases of placenta praevia treated largely along conservative lines is reported ; there were no maternal deaths, and the foetal and neonatal loss was 16.5%, which compares favourably with other recently reported figures.

The causes of foetal death in this series are analysed ; the majority would appear to have been avoidable.

Conclusions are drawn regarding the present scope of conservative treatment.

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